IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Yasuo OHTSUKA et al. :

Serial No. NEW : **Attn: Application Branch**

Filed February 13, 2002 : **Attorney Docket No. 2002_0194**

TRICYCLIC TRIAZOLOBENZAZEPINE DERIVATIVES, PROCESS FOR PRODUCING THE SAME, AND ANTIALLERGIC AGENTS
(Rule 1.53(b) Divisional of Serial No. 09/509,494, Filed March 29, 2000)

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, DC 20231

Sir:

Please amend the above-identified application as follows:

IN THE SPECIFICATION

Page 1, after the title of the invention, please insert the following paragraph:

This application is a divisional application of Serial No. 09/509,494 filed March 29, 2000, now allowed, which is a 371 application of PCT/JP98/04363 filed September 29, 1998.

Please rewrite the paragraphs from page 19, line 27 to page 20, line 3 as follows:

R^{41} and R^{42} represent preferably C_{1-4} alkoxy, more preferably methoxy or isopropyloxy. Still more preferably, R^{41} represents methoxy, and R^{42} represents methoxy or isopropyloxy.

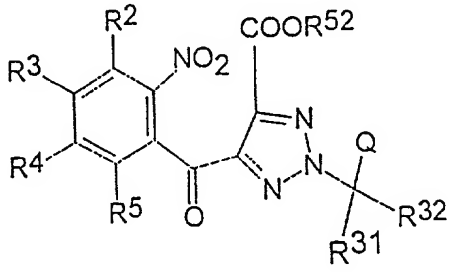
A group of preferred compounds represented by formula (Ia) include a group of compounds wherein R^{41} and R^{42} represent C_{1-6} alkoxy (preferably C_{1-4} alkoxy, more preferably methoxy or isopropyloxy), and Q represents group (i) (preferably, R^{33} represents optionally C_{1-4} alkoxy-substituted C_{1-4} alkyl).

IN THE CLAIMS

Cancel, without prejudice to the subject matter involved, claims 1-18.

Please amend claims 19-30 as follows:

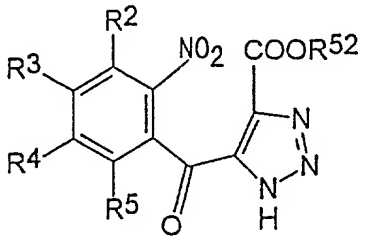
19. (Amended) A process for preparing a compound represented by formula (IIa')



(II a')

wherein Q represents group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the steps of:

(1) reacting a compound represented by formula (V)



(V)

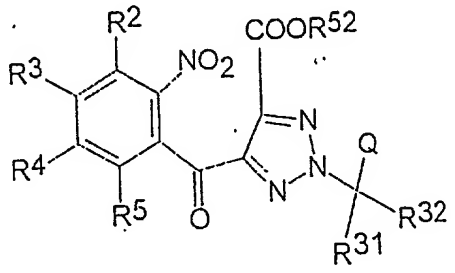
wherein R^2 to R^5 and R^{52} are as defined above,

with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined above in claim 1;

(2) reacting the compound prepared in step (1) with a compound represented by R^{71}-C(=O)-R^{72} wherein R^{71} and R^{72} each independently represent a chlorine atom, 4-nitrophenyl, or 1-imidazolyl; and

(3) reacting the compound prepared in step (2) with a compound represented by $R^{33}OH$ wherein R^{33} is as defined in claim 1.

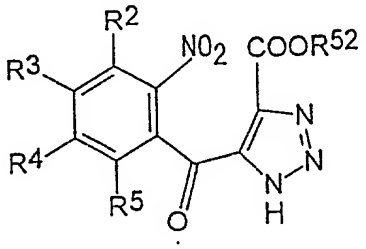
20. (Amended) A process for preparing a compound represented by formula (IIa')



(II a')

wherein Q represents the group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the steps of:

(1) reacting a compound represented by formula (V)



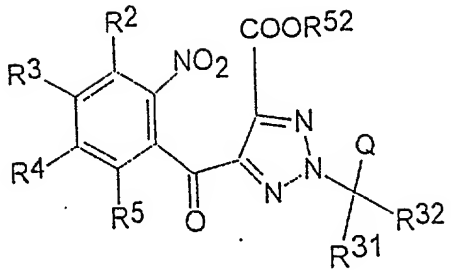
(V)

wherein R^2 to R^5 and R^{52} are as defined above,

with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1; and

(2) reacting the compound prepared in step (1) with a compound represented by $HalCOOR^{33}$ wherein Hal represents a halogen atom and R^{33} is as defined in claim 1, in the presence of an alkali metal carbonate and an alkali metal iodide.

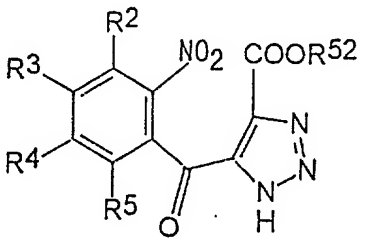
21. (Amended) A process for preparing a compound represented by formula (IIa')



(II a')

wherein Q represents group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the step of

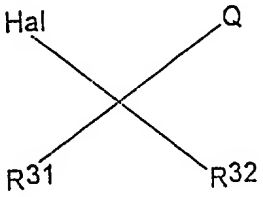
reacting a compound represented by formula (V)



(V)

wherein R^2 to R^5 and R^{52} are as defined above,

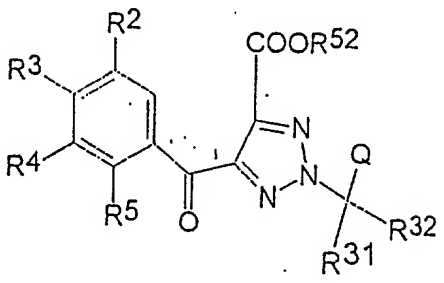
with a compound represented by formula (IV)



(IV)

wherein Hal represents a halogen atom, Q represents the group (i) as defined in claim 1, and R^{31} and R^{32} are as defined above, in the presence of an inorganic base and an alkali metal iodide.

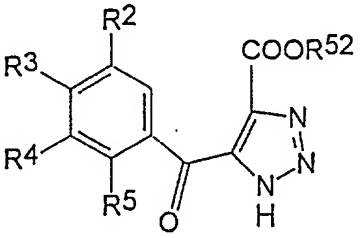
22. (Amended) A process for producing a compound represented by formula (VI')



(VI ')

wherein Q represents the group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the steps of:

(1) reacting a compound represented by formula (VII)



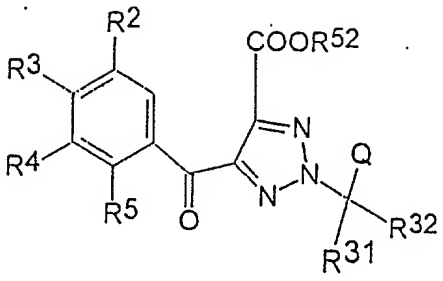
(VII)

wherein R^2 to R^5 and R^{52} are as defined above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1;

(2) reacting the compound prepared in step (1) with a compound represented by R^{71}-C(=O)-R^{72} wherein R^{71} and R^{72} each independently represent a chlorine atom, 4-nitrophenyl, or 1-imidazolyl; and

(3) reacting the compound prepared in step (2) with a compound represented by $R^{33}OH$ wherein R^{33} is as defined in claim 1.

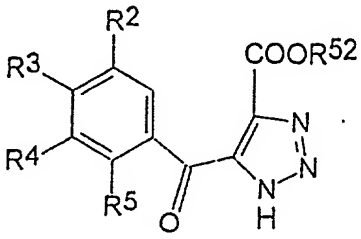
23. (Amended) A process for preparing a compound represented by formula (VI')



(VI ')

wherein Q represents group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the steps of:

(1) reacting a compound represented by formula (VII)

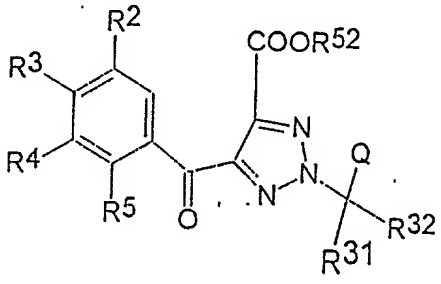


(VII)

wherein R^2 to R^5 and R^{52} are as defined above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1; and

(2) reacting the compound prepared in step (1) with a compound represented by $HalCOOR^{33}$ wherein Hal represents a halogen atom and R^{33} is as defined in claim 1, in the presence of an alkali metal carbonate and an alkali metal iodide.

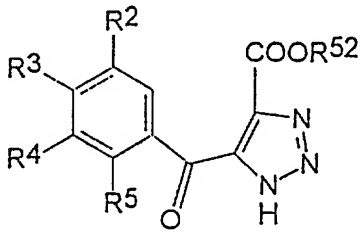
24. (Amended) A process for producing a compound represented by formula (VI')



(VI ')

wherein Q represents group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined above, which comprises the step of

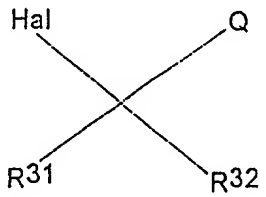
reacting a compound represented by formula (VII)



(VII)

wherein R^2 to R^5 and R^{52} are as defined above,

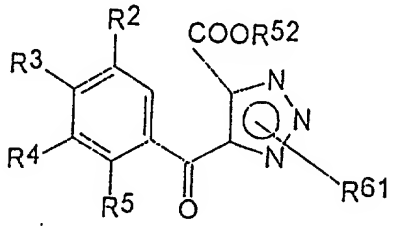
with a compound represented by formula (IV)



(IV)

wherein Hal represents a halogen atom, Q represents the group (i) as defined in claim 1, and R^{31} and R^{32} are as defined above, in the presence of an inorganic base and an alkali metal iodide.

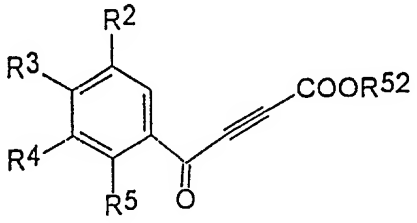
25. (Amended) A process for preparing a compound represented by formula (VIII)



(VIII)

wherein R^2 to R^5, R^{52}, and R^{61} are as defined above, which comprises the step of

(a) reacting a compound represented by formula (IX)



(IX)

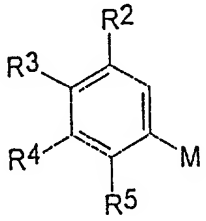
wherein R^2 to R^5 and R^{52} are as defined above,

with a compound represented by formula (X)

R^{61}-N_3 (X)

wherein R^{61} is as defined above, or

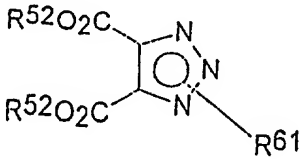
(b) reacting a compound represented by formula (XII)



(XII)

wherein M represents lithium, magnesium chloride, magnesium bromide, magnesium iodide, zinc bromide, zinc iodide, cadmium bromide, iodide cadmium, or copper and R^2 to R^5 are as defined in claim 1,

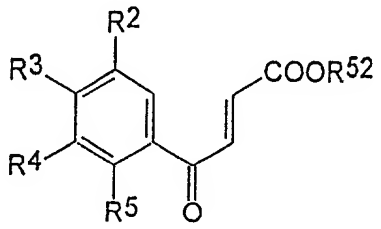
with a compound represented by formula (XIII)



(XIII)

wherein R^{52} and R^{61} are as defined above.

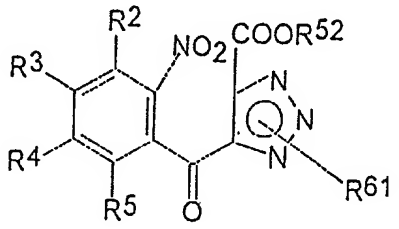
26. (Amended) A process according to claim 25, which further comprises the step of, prior to the reaction of the compound represented by formula (IX) with the compound represented by formula (X) in step (a), dehydrogenating a compound represented by formula (XI)



(XI)

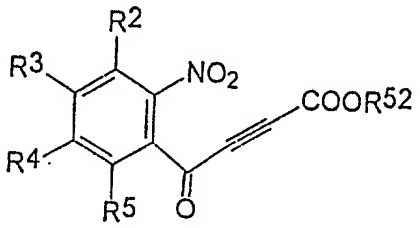
wherein R^2 to R^5 and R^{52} are as defined above,
to produce the compound represented by formula (IX).

27. (Amended) A process for producing a compound represented by formula (XV)



(XV)

wherein R^2 to R^5, R^{52}, and R^{61} are as defined above, which comprises the step of
reacting a compound represented by formula (XVI)



(XVI)

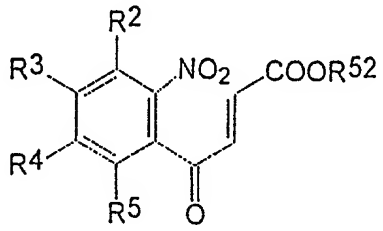
wherein R^2 to R^5, and R^{52} are as defined above,

with a compound represented by formula (X)

$$R^{61}\text{-}N_3 \qquad (X)$$

wherein R^{61} is as defined in claim 18.

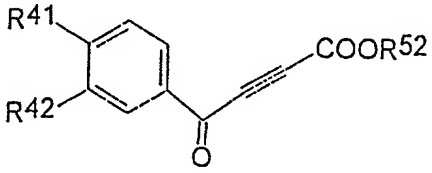
28. (Amended) A process according to claim 27, which further comprises the step of, prior to the reaction of the compound represented by formula (XVI) with the compound represented by formula (X), a compound represented by formula (XVII)



(XVII)

wherein R^2 to R^5 and R^{52} are as defined above,
is dehydrogenated to produce the compound represented by formula (XVI).

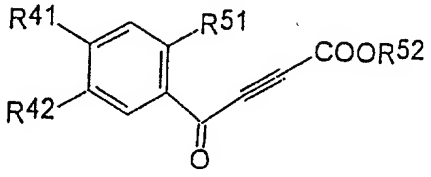
29. (Amended) A compound represented by formula (IXa) or a salt or solvate thereof



(IXa)

wherein R^{41}, R^{42}, and R^{52} are as defined in claim 6, provided that R^{41} and/or R^{42} do not represent a hydrogen atom.

30. (Amended) A compound represented by formula (XVIa) or a salt or solvate thereof

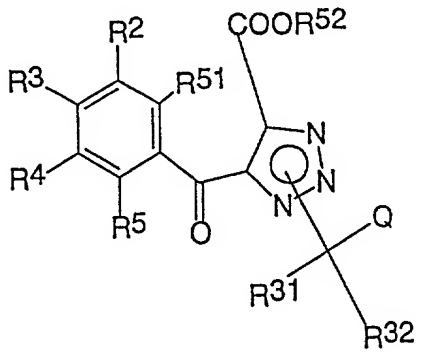


(XVIa)

wherein R^{41}, R^{42}, R^{51}, and R^{52} are as defined in claim 6.

Please add new claims 31-36 as follows:

31. (New) A compound represented by formula (II) or a salt or solvate thereof:



(II)

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

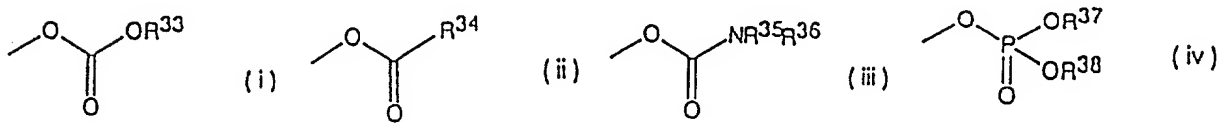
(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl;

R^{31} and R^{32}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a halogen atom; and

Q represents a group selected from the following groups (i) to (iv) or a halogen atom or C_{1-6} alkoxy:



wherein

R^{33} represents

C_{1-6} alkyl which may be substituted by C_{1-6} alkoxy optionally substituted by C_{1-6} alkoxy, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

R^{33} may form C_{1-4} alkylene together with R^{31} or R^{32},

R^{34} represents

C_{1-16} alkyl which may be substituted by a halogen atom, carboxyl, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro,

R^{35} and R^{36}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be

substituted by amino optionally substituted by C_{1-4} alkyl or

R^{35} and R^{36} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached, and

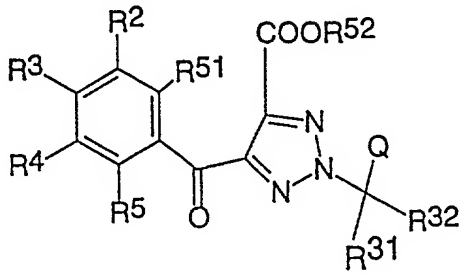
R^{37} and R^{38}, which may be the same or different, represent C_{1-6} alkyl,

R^{51} represents nitro or amino, and

R^{52} represents a hydrogen atom or a protective group for carboxyl,

provided that the group $-CR^{31}R^{32}Q$ does not represent C_{1-6} alkyl substituted by a halogen atom or C_{1-6} alkoxy.

32. (New) A compound represented by formula (II') or a salt or solvate thereof:



(II')

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

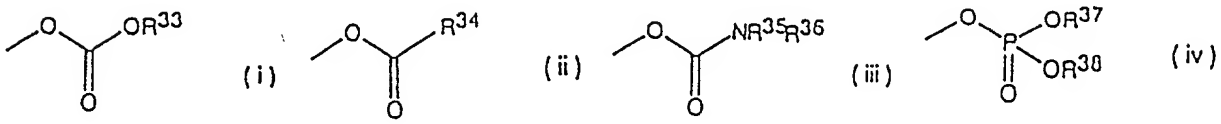
(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl;

R^{31} and R^{32}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a halogen atom; and

Q represents a group selected from the following groups (i) to (iv) or a halogen atom or C_{1-6} alkoxy:



wherein

R^{33} represents

C_{1-6} alkyl which may be substituted by C_{1-6} alkoxy optionally substituted by C_{1-6} alkoxy, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

R^{33} may form C_{1-4} alkylene together with R^{31} or R^{32},

R^{34} represents

C_{1-16} alkyl which may be substituted by a halogen atom, carboxyl, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro,

R^{35} and R^{36}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be

substituted by amino optionally substituted by C_{1-4} alkyl or

R^{35} and R^{36} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached, and

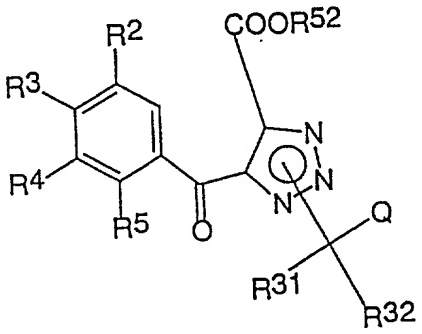
R^{37} and R^{38}, which may be the same or different, represent C_{1-6} alkyl,

R^{51} represents nitro or amino, and

R^{52} represents a hydrogen atom or a protective group for carboxyl,

provided that the group $-CR^{31}R^{32}Q$ does not represent C_{1-6} alkyl substituted by a halogen atom or C_{1-6} alkoxy.

33. (New) A compound represented by formula (VI) or a salt or solvate thereof:



(VI)

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

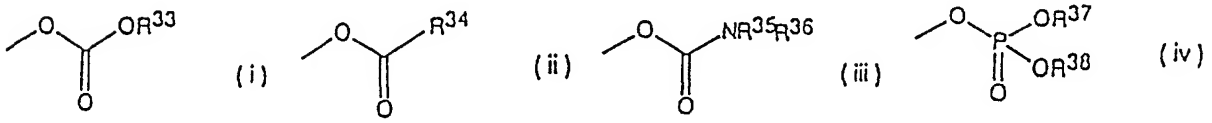
(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl;

R^{31} and R^{32}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a halogen atom; and

Q represents a group selected from the following groups (i) to (iv) or a halogen atom or C_{1-6} alkoxy:



(i) (ii) (iii) (iv)

wherein

R^{31} represents

C_{1-6} alkyl which may be substituted by C_{1-6} alkoxy optionally substituted by C_{1-6} alkoxy, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

R^{31} may form C_{1-4} alkylene together with R^{31} or R^{32},

R^{34} represents

C_{1-16} alkyl which may be substituted by a halogen atom, carboxyl, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro,

R^{35} and R^{36}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be

substituted by amino optionally substituted by C_{1-4} alkyl or

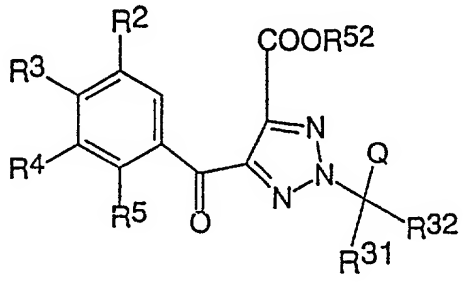
R^{35} and R^{36} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached, and

R^{37} and R^{38}, which may be the same or different, represent C_{1-6} alkyl,

R^{52} represents a hydrogen atom or a protective group for carboxyl,

provided that the group $-CR^{31}R^{32}Q$ does not represent C_{1-6} alkyl substituted by a halogen atom or C_{1-6} alkoxy.

34. (New) A compound represented by formula (VI') or a salt or solvate thereof:



(VI')

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

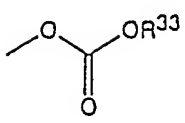
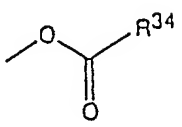
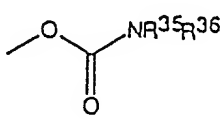
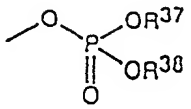
(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl;

R^{31} and R^{32}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a halogen atom; and

Q represents a group selected from the following groups (i) to (iv) or a halogen atom or C_{1-6} alkoxy:


(i)

(ii)

(iii)

(iv)

wherein

R^{33} represents

C_{1-6} alkyl which may be substituted by C_{1-6} alkoxy optionally substituted by C_{1-6} alkoxy, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

R^{33} may form C_{1-4} alkylene together with R^{31} or R^{32},

R^{34} represents

C_{1-16} alkyl which may be substituted by a halogen atom, carboxyl, phenyl optionally substituted by C_{1-6} alkoxy, amino, or nitro, or a saturated or unsaturated five- to seven-membered heterocyclic ring optionally substituted by C_{1-6} alkoxy, amino, or nitro,

phenyl which may be substituted by C_{1-6} alkoxy, amino, or nitro, or

a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-6} alkoxy, amino, or nitro,

R^{35} and R^{36}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be

substituted by amino optionally substituted by C_{1-4} alkyl or

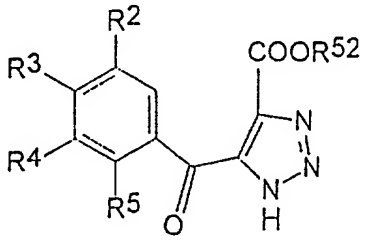
R^{35} and R^{36} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached, and

R^{37} and R^{38}, which may be the same or different, represent C_{1-6} alkyl,

R^{52} represents a hydrogen atom or a protective group for carboxyl,

provided that the group $-CR^{31}R^{32}Q$ does not represent C_{1-6} alkyl substituted by a halogen atom or C_{1-6} alkoxy.

35. (New) A compound represented by formula (VII) or a salt or solvate thereof:



(VII)

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

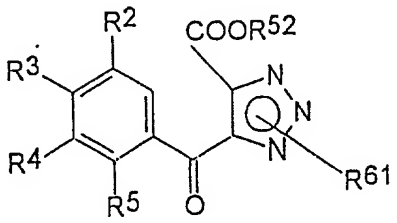
(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl; and

R^{52} represents a hydrogen atom or a protective group for carboxyl.

36. (New) A compound represented by formula (VIII) or a salt or solvate thereof:



(VIII)

wherein R^2, R^3, R^4, and R^5, which may be the same or different, represent any one of the following (a) to (n):

(a) a hydrogen atom;

(b) a halogen atom;

(c) an optionally protected hydroxyl group;

(d) formyl;

(e) C_{1-12} alkyl which may be substituted by a halogen atom;

(f) C_{2-12} alkenyl which has one or more carbon-carbon double bonds and may be substituted by

(1) a halogen atom,

(2) cyano,

(3) $-COR^9$ wherein R^9 represents a hydrogen atom or C_{1-6} alkyl,

(4) $-COOR^{10}$ wherein R^{10} represents a hydrogen atom or C_{1-6} alkyl,

(5) $-CONR^{11}R^{12}$ wherein R^{11} and R^{12}, which may be the same or different, represent

(i) a hydrogen atom,

(ii) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl, phenyl optionally substituted by C_{1-4} alkyl which may be substituted by a saturated five- to seven-membered heterocyclic ring containing one or two nitrogen atoms (the

nitrogen atoms may be substituted by C_{1-4} alkyl), or a saturated or unsaturated five- to seven-membered heterocyclic ring,

(iii) phenyl which may be substituted by carboxyl, or

(iv) a saturated or unsaturated five to seven-membered heterocyclic ring,

(6) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or may form a bicyclic ring fused with another ring;

(g) C_{1-12} alkoxy which may be substituted by

(1) a halogen atom,

(2) a hydroxyl group,

(3) cyano,

(4) C_{3-7} cycloalkyl,

(5) phenyl,

(6) C_{1-4} alkoxy,

(7) phenoxy,

(8) amino which may be substituted by C_{1-4} alkyl,

(9) $-COR^{13}$ wherein R^{13} represents a hydrogen atom, C_{1-6} alkyl, phenyl optionally substituted by halogen or C_{1-4} alkoxy, or phenyl C_{1-4} alkyl,

(10) $-COOR^{14}$ wherein R^{14} represents a hydrogen atom or C_{1-6} alkyl,

(11) $-CONR^{15}R^{16}$ wherein R^{15} and R^{16}, which may be the same or different, represent a hydrogen atom or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or

(12) a saturated or unsaturated five- to seven-membered heterocyclic ring which may be substituted by C_{1-4} alkyl or phenyl C_{1-4} alkyl;

(h) $-C=N-OR^{16a}$ wherein R^{16a} represents a hydrogen atom, C_{1-6} alkyl, phenyl C_{1-4} alkyl, or phenyl;

(i) $-(CH_2)mOR^{17}$ wherein m is an integer of 0 to 4, and R^{17} represents a hydrogen atom, C_{1-6} alkyl, or phenyl C_{1-4} alkyl of which one or more hydrogen atoms on the benzene ring may be substituted by C_{1-4} alkyl;

(j) $-(CH_2)k-COR^{18}$ wherein k is an integer of 1 to 4, and R^{18} represents a hydrogen atom or C_{1-4} alkyl;

(k) $-(CH_2)j-COOR^{19}$ wherein j is an integer of 0 to 4, and R^{19} represents a hydrogen atom or C_{1-6} alkyl;

(l) $-(CH_2)p-NR^{20}R^{21}$ wherein p is an integer of 1 to 4, and R^{20} and R^{21}, which may be the same or different, represent

(1) a hydrogen atom,

(2) C_{1-6} alkyl which may be substituted by amino optionally substituted by C_{1-4} alkyl,

(3) phenyl C_{1-4} alkyl,

(4) $-COR^{22}$ wherein R^{22} represents a hydrogen atom or C_{1-4} alkyl which may be substituted by carboxyl, or

(5) $-SO_2R^{23}$ wherein R^{23} represents C_{1-4} alkyl or phenyl which may be substituted by a halogen atom;

(m) $-(CH_2)q-CONR^{24}R^{25}$ wherein q is an integer of 0 to 4, and R^{24} and R^{25}, which may be the same or different, represent a hydrogen atom, a saturated or unsaturated

five- to seven-membered heterocyclic ring, or C_{1-6} alkyl which may be substituted by a saturated or unsaturated five- to seven-membered heterocyclic ring, or alternatively R^{24} and R^{25} may form a saturated or unsaturated five- to seven-membered heterocyclic ring together with a nitrogen atom to which they are attached (the heterocyclic ring may further contain at least one oxygen, nitrogen, or sulfur atom, may form a bicyclic ring fused with another ring, or may be substituted by C_{1-4} alkyl); and

(n) $-NR^{26}R^{27}$ wherein R^{26} and R^{27}, which may be the same or different, represent a hydrogen atom or $-COR^{28}$ wherein R^{28} represents a hydrogen atom, C_{1-6} alkyl, or phenyl which may be substituted by C_{1-4} alkyl or C_{1-6} alkoxy optionally substituted by phenyl;

R^{52} represents a hydrogen atom or a protective group for carboxyl; and

R^{61} represents a protective group for triazole.

Please replace the original Abstract with the new Abstract on the separate sheet submitted herewith.

REMARKS

The present application is being filed as a result of a restriction requirement in the parent application, for which a Notice of Allowance was issued November 30, 2001. The present divisional application is directed to the non-elected subject matter of original claims 13-30.

The specification has been amended to insert a cross-reference to the parent application and the international application on which the parent application is based. The specification has been further amended in the same manner as in the parent application. None of these amendments was objected to by the Examiner as constituting new matter.

Claims 19-30 have been amended to avoid their multiple dependency, to reduce the filing fee.

The Abstract has been amended to insert a period at the end, as required by the Examiner in the parent application.

Attached hereto is a marked-up version of the changes made to the Specification, claims and Abstract by the current amendment. The attached pages are captioned "**Version with markings to show changes made.**"

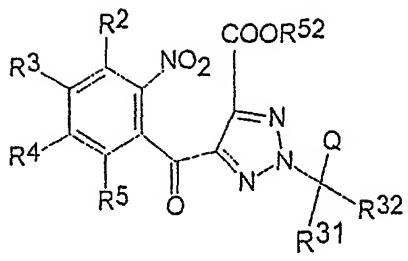
Claims 1-18 have been canceled, and new claims 31-36 have been added to the application. These new claims correspond to original claims 13-18 in independent form. Applicants note that the subject matter from claim 1 incorporated into the new claims is taken from allowed claim 1 of the parent application.

Respectfully submitted,

Yasuo OHTSUKA et al.

By _____
Michael R. Davis
Registration No. 25,134
Attorney for Applicants

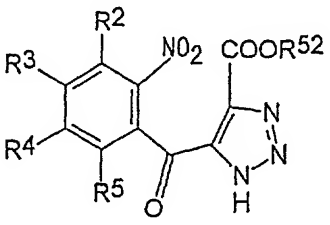
MRD/aeh
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
February 13, 2002



(II a')

wherein Q represents group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the steps of:

(1) reacting a compound represented by formula (V)



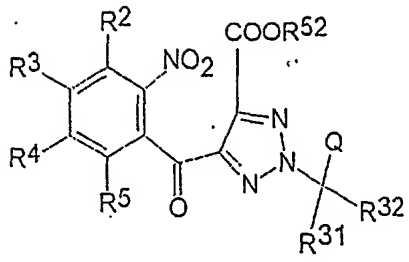
(V)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined above in claim 1;

(2) reacting the compound prepared in step (1) with a compound represented by R^{71}-C(=O)-R^{72} wherein R^{71} and R^{72} each independently represent a chlorine atom, 4-nitrophenyl, or 1-imidazolyl; and

(3) reacting the compound prepared in step (2) with a compound represented by $R^{33}OH$ wherein R^{33} is as defined in claim 1.

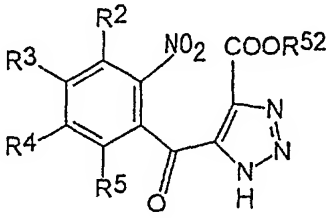
20. A process for preparing a compound represented by formula (IIa')



(IIa')

wherein Q represents the group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the steps of:

(1) reacting a compound represented by formula (V)

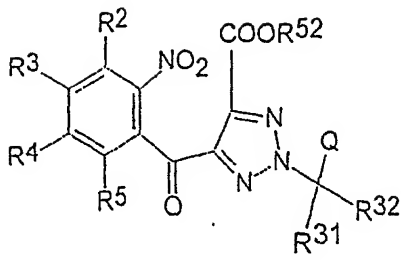


(V)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1; and

(2) reacting the compound prepared in step (1) with a compound represented by $HalCOOR^{33}$ wherein Hal represents a halogen atom and R^{33} is as defined in claim 1, in the presence of an alkali metal carbonate and an alkali metal iodide.

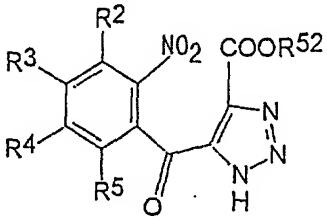
21. A process for preparing a compound represented by formula (IIa')



(II a')

wherein Q represents group (i) as defined in claim 1 and R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the step of

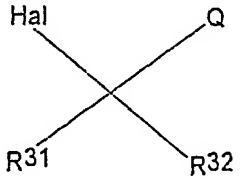
reacting a compound represented by formula (V)



(V)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above,

with a compound represented by formula (IV)

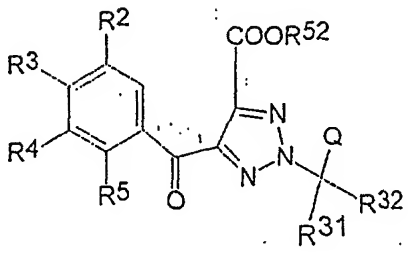


(IV)

wherein Hal represents a halogen atom, Q represents the group (i) as defined in claim 1, and R^{31} and R^{32} are as defined above, in the presence of an inorganic base and an alkali metal iodide.

22. A process for producing a compound

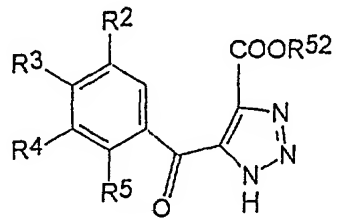
represented by formula (VI')



(VI')

wherein Q represents the group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the steps of:

(1) reacting a compound represented by formula (VII).



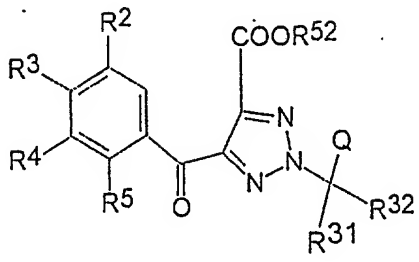
(VII)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1;

(2) reacting the compound prepared in step (1) with a compound represented by $R^{71}-C(=O)-R^{72}$ wherein R^{71} and R^{72} each independently represent a chlorine atom, 4-nitrophenyl, or 1-imidazolyl; and

(3) reacting the compound prepared in step (2) with a compound represented by $R^{33}OH$ wherein R^{33} is as defined in claim 1.

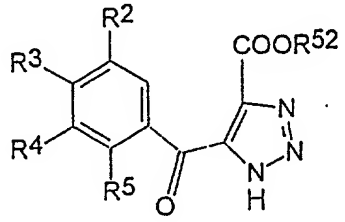
23. A process for preparing a compound represented by formula (VI')



(VI')

wherein Q represents group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the steps of:

(1) reacting a compound represented by formula (VII)

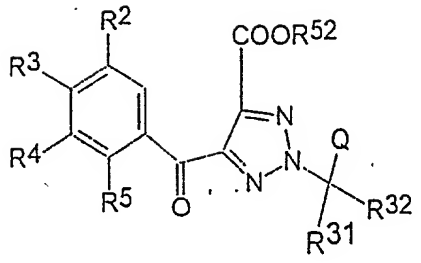


(VII)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above, with a compound represented by $R^{31}R^{32}C=O$ wherein R^{31} and R^{32} are as defined in claim 1; and

(2) reacting the compound prepared in step (1) with a compound represented by $HalCOOR^{33}$ wherein Hal represents a halogen atom and R^{33} is as defined in claim 1, in the presence of an alkali metal carbonate and an alkali metal iodide.

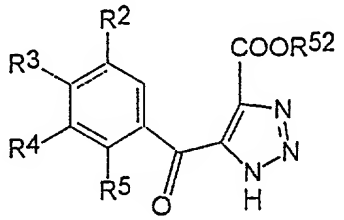
24. A process for producing a compound represented by formula (VI')



(VI')

wherein Q represents group (i) as defined in claim 1, R^2 to R^5, R^{31}, R^{32}, and R^{52} are as defined ~~in claims 1 and 13~~ above, which comprises the step of

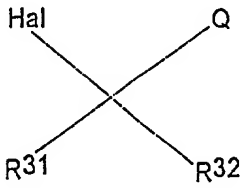
reacting a compound represented by formula (VII)



(VII)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above

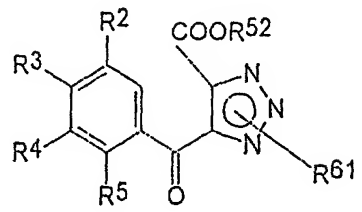
with a compound represented by formula (IV)



(IV)

wherein Hal represents a halogen atom, Q represents the group (i) as defined in claim 1, and R^{31} and R^{32} are as defined above, in the presence of an inorganic base and an alkali metal iodide.

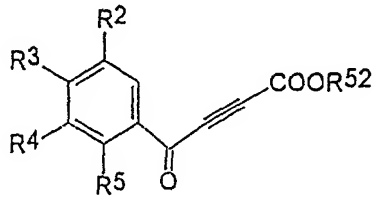
25. A process for preparing a compound represented by formula (VIII)



(VIII)

wherein R^2 to R^5, R^{52}, and R^{61} are as defined ~~in claims 1, 13, and 18~~ above, which comprises the step of

(a) reacting a compound represented by formula (IX)



(IX)

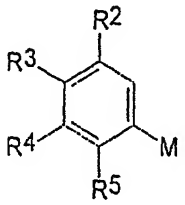
wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above,

with a compound represented by formula (X)

$R^{61}-N_3$ (X)

wherein R^{61} is as defined ~~in claim 18~~ above, or

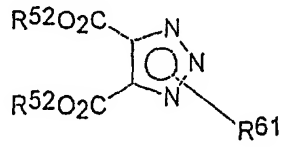
(b) reacting a compound represented by formula (XII)



(XII)

wherein M represents lithium, magnesium chloride, magnesium bromide, magnesium iodide, zinc bromide, zinc iodide, cadmium bromide, iodide cadmium, or copper and R^2 to R^5 are as defined in claim 1,

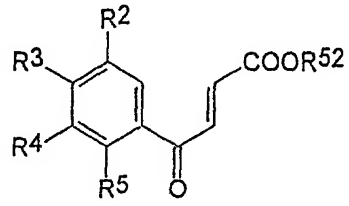
with a compound represented by formula (XIII)



(XIII)

wherein R^{52} and R^{61} are as defined ~~in claims 13 and 18~~ above.

26. A process according to claim 25, which further comprises the step of, prior to the reaction of the compound represented by formula (IX) with the compound represented by formula (X) in step (a), dehydrogenating a compound represented by formula (XI)

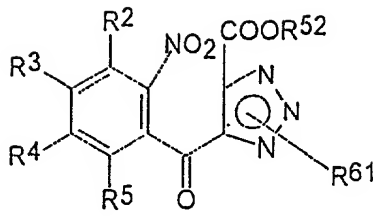


(XI)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 18~~ above,

to produce the compound represented by formula (IX).

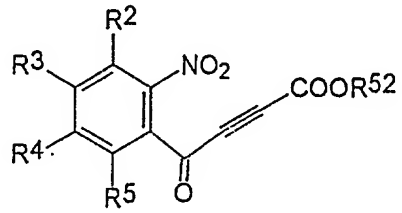
27. A process for producing a compound represented by formula (XV)



(XV)

wherein R^2 to R^5, R^{52}, and R^{61} are as defined ~~in claims 1, 13 and 18~~ above, which comprises the step of

reacting a compound represented by formula (XVI)



(XVI)

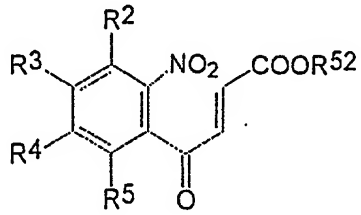
wherein R^2 to R^5, and R^{52} are as defined ~~in claims 1 and 13~~ above,

with a compound represented by formula (X)

$R^{61}-N_3$ (X)

wherein R^{61} is as defined in claim 18.

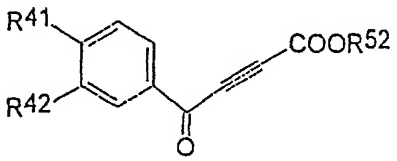
28. A process according to claim 27, which further comprises the step of, prior to the reaction of the compound represented by formula (XVI) with the compound represented by formula (X), a compound represented by formula (XVII)



(XVII)

wherein R^2 to R^5 and R^{52} are as defined ~~in claims 1 and 13~~ above, is dehydrogenated to produce the compound represented by formula (XVI).

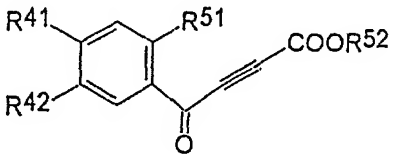
29. A compound represented by formula (IXa) or a salt or solvate thereof



(IXa)

wherein R^{41}, R^{42}, and R^{52} are as defined ~~above~~ in claims 6 ~~and 13~~, provided that R^{41} and/or R^{42} do not represent a hydrogen atom.

30. A compound represented by formula (XVIa) or a salt or solvate thereof

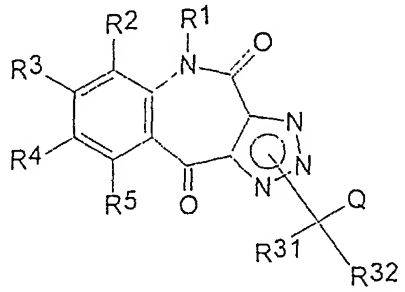


(XVIa)

wherein R^{41}, R^{42}, R^{51}, and R^{52} are as defined in claims 6 ~~and 13~~.

ABSTRACT

Tricyclic triazolobenzazepine derivatives in the form of a prodrug are provided. The compounds according to the present invention are those represented by formula (I) and pharmacologically acceptable salts and solvates thereof. The compounds are useful as antiallergic agents and exhibit excellent bioavailability.

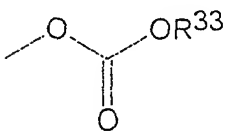


(I)

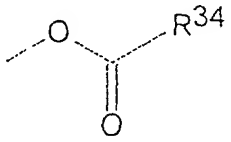
wherein R^1 represents hydrogen, OH, alkyl or phenyl alkyl,

R^2, R^3, R^4, and R^5 represent hydrogen, halogen, optionally protected hydroxyl, formyl, optionally substituted alkyl, alkenyl, alkoxy or the like, and

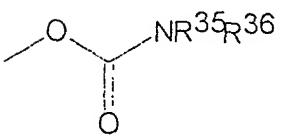
Q represents a group selected from the following groups (i) to (iv), halogen, or alkoxy:



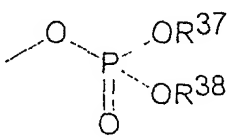
(i) ;



(ii) ;



(iii)

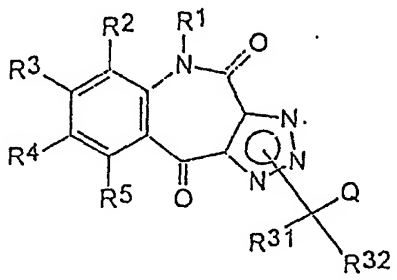


(iv)

; and

ABSTRACT

Tricyclic triazolobenzazepine derivatives in the form of a prodrug are provided. The compounds according to the present invention are those represented by formula (I) and pharmacologically acceptable salts and solvates thereof. The compounds are useful as antiallergic agents and exhibit excellent bioavailability.

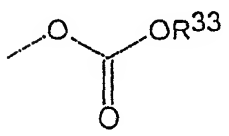


(I)

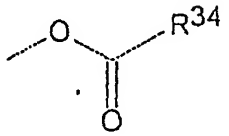
wherein R^1 represents hydrogen, OH, alkyl or phenyl alkyl,

R^2, R^3, R^4, and R^5 represent hydrogen, halogen, optionally protected hydroxyl, formyl, optionally substituted alkyl, alkenyl, alkoxy or the like, and

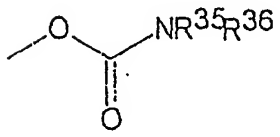
Q represents a group selected from the following groups (i) to (iv), halogen, or alkoxy:



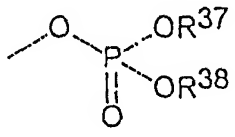
(i) ;



(ii) ;



(iii) ;



(iv) ; and

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please rewrite the paragraphs from page 19, line 27 to page 20, line 3 as follows:

R^{41} and R^{42} represent preferably C_{1-4} alkoxy, more preferably methoxy or isopropyloxy [isopropyl]. Still more preferably, R^{41} represents methoxy, and R^{42} represents methoxy or isopropyloxy [isopropyl].

A group of preferred compounds represented by formula (Ia) include a group of compounds wherein R^{41} and R^{42} represent C_{1-6} alkoxy (preferably C_{1-4} alkoxy, more preferably methoxy or isopropyloxy [isopropyl]), and Q represents group (i) (preferably, R^{33} represents optionally C_{1-4} alkoxy-substituted C_{1-4} alkyl).

19. A process for preparing a compound represented by formula (IIa')